C. Remarks/Argument

Reconsideration of this application is respectfully requested. Upon entry of the amendments, claims 1-55 will be pending. Claim 1 has been amended herein to address the Examiner's rejections and to more particularly point out and distinctly claim the invention. Claims 8, 11-14, and 16-55 are withdrawn as directed to nonelected inventions. Applicants hereby request rejoinder of these withdrawn claims, which have been amended herein to depend from a corresponding composition claim. *See* MPEP §821.04 and 37 C.F.R. § 1.104. Applicants address the Examiner's comments below.

Novelty

Claims 1, 4, and 5 are rejected as anticipated by Avrahami et al., Biochem 41, 2254-63, 2002 ("Avrahami"). Specifically, the Examiner contends that Avrahami discloses that palmitic and undecanoic conjugates of a magainin analog (GIGKFLHSAKKWGKAFVGEIMNS-NH_2) inhibits fungal growth and thus anticipates claims 1, 4, and 5. Applicants traverse as the rejection may apply to the claims as amended.

Claim 1 (from which claims 4 and 5 directly depend) has been amended herewith to recite a lipophilic conjugate comprising a peptide coupled to a fatty acid. The peptide comprises at least two positively charged amino acid residues, such that the peptide has a net positive charge that is equal to or greater than +1, and wherein the peptide after conjugation to the fatty acid has at least one activity selected from the group consisting of antibacterial, antifungal, and anticancer activity, such that the activity of the peptide after conjugation to the fatty acid is

higher than the activity of the peptide prior to conjugation to the fatty acid, the peptide prior to conjugation being devoid or having very weak antibacterial and antifungal activity.

Avrahami explicitly discloses that magainin is a well-characterized antibacterial peptide (see the Abstract and p. 2255, left column, lines 9-10 of Avrahami). Avrahami further discloses that magainin has poor antifungal activity and that conjugation of a lipophilic acid to magainin endowed the peptide with anti-fungal activity. Thus, according to Avrahami while magainin has poor antifungal activity, it does have high antibacterial activity.

In contrast, the peptides of the present invention are devoid or possess very weak antimicrobial activity prior to conjugation to a fatty acid. The peptides of the present invention are thus distinct from magainin. In order to distinguish the peptides of the present invention from magainin, claim 1 has been amended to include the limitation that the peptide is devoid or possess very weak antibacterial and antifungal activity before conjugation to a fatty acid. Support for the amendment can be found at paragraphs [0014], [0018], and [0022] of the currently published application (US 2007/0072808). Accordingly, the teachings of Avrahami do not meet each and every limitation of claim 1, and the reference cannot be said to anticipate the claim. Thus, the rejection should be withdrawn.

Similarly, because claims 4 and 5 depend from claim 1 and necessarily incorporate all the limitations thereof, Avrahami cannot anticipate claims 4 and 5. Reconsideration and withdrawal of the rejections are requested.

Claims 1 and 4 are also rejected as anticipated by U.S. Patent No. 3,817,973 to Bouchaudon ("Bouchaudon"). According to the Examiner, Bouchaudon anticipates claims 1 and 4 because it discloses compounds of the following formula (which are cyclized):

A-X-Dab-Thr-Dab-Dab-Dab-Y-Z-Dab-Dab-Thr,

which exhibit antibacterial activity. Applicants traverse as the rejection may apply to the claims as amended.

The lipophilic conjugate recited by claim 1 as amended comprises a peptide having a net positive charge that is equal or greater than +1, and at least two positively charged amino acid residues.

In contrast, Bouchaudon discloses polymoxins that do not have a net positive charge that is equal to or greater than +1 and that do not include at least two positively charged amino acid residues. Rather, the peptide of Bouchaudon consists of Dab, Thr, and one of the chains D-Phe-Leu, D-Leu-Leu, and D-Leu-Ile. However, none of these amino acids is basic or positively charged. Accordingly, the teachings of Bouchaudon do not meet each and every limitation of claim 1. Therefore, the reference cannot be said to anticipate claim 1 and the rejection should be withdrawn. Reconsideration and withdrawal are respectfully requested.

Obviousness

Claims 1 and 4 are also rejected as obvious in view of each of U.S. Patent No. 7,262,268 to Morytko et al. ("Morytko") and U.S. Patent No. 6,794,490 to Hill et al.

("Hill") under 35 U.S.C. § 103(a). According to the Examiner, Morytko and Hill each disclose various antibacterial peptides that bear an acyl group and that have at least two amino acid side chains that are sufficiently basic to become protonated. Applicants traverse as the rejections may be applied to the claims as amended.

As previously indicated, Claim 1 has been amended herewith to recite a lipophilic conjugate comprising a peptide coupled to a fatty acid. The peptide comprises at least two positively charged amino acid residues, such that the peptide has a net positive charge that is equal to or greater than +1, and wherein the peptide after conjugation to the fatty acid has at least one activity selected from the group consisting of antibacterial, antifungal, and anticancer activity, such that the activity of the peptide after conjugation to the fatty acid is higher than the activity of the peptide prior to conjugation to the fatty acid, the peptide prior to conjugation being devoid or having very weak antibacterial and antifungal activity.

The term "positively charged amino acid" as used in the instant application has its common and known meaning, namely basic amino acids in which the R groups have a net positive charge at pH 6.0 to 7.0 (see paragraphs [0063] of the published application and Biochemistry, Lehninger A.L. ed., Worth Publishers, Inc. 1976). In addition, negatively charged amino acids are acidic amino acids in which the R group has a net negative charge at pH 6.0 to 7.0 (see paragraphs [0063] of the published application and Biochemistry, Lehninger A.L. ed., Worth Publishers, Inc. 1976). Thus, the peptides of the present invention are basic peptides having a net positive charge that is equal or higher than +1 at pH 6.0 to 7.0. The positive charge of the peptides of the current

invention is due to the amino acid composition of the peptide (paragraph [0062] of the published application) and not due to the pH in the stomach.

The peptides disclosed in Morytko are daptomycin compounds, all of which are well-known acidic peptide antibiotics (see col. 2, lines 34-35 of U.S. Patent No. 4,537,717 to Abbott cited in Morytko and col. 2, lines 35-50 of U.S. Patent No. 4,208,403). The peptides disclosed by Morytko include five acidic or negatively charged amino acids (i.e., aspartic acids and a glutamic acid derivative), and one basic or positively charged amino acid (ornithine). The peptide moieties of the lipopeptides disclosed by Hill show similarity to the peptides disclosed by Morytko. In contrast to the peptides used in the present invention, the peptides disclosed by Morytko and Hill are acidic (*i.e.*, include an excess of negatively charged amino acids) and hence their net charge is lower than +1. Thus, Morytko and Hill teach away from the claimed invention as amended.

Accordingly, the claims as amended recite novel distinctions over each of Morytko and Hill, which distinctions are unobvious. Thus, reconsideration and withdrawal of the rejection is respectfully requested.

For all of the foregoing reasons, and in view of the amendments to the claims, Applicants request withdrawal of the rejections under 35 U.S.C. §§ 102 and 103. Applicants submit that this paper is fully responsive and action on the merits of the product claims and a Notice of Allowance thereof are respectfully requested. Similarly, because Applicants have herein requested rejoinder of the withdrawn claims and have amended those claims to be dependent

upon the product claims herein, a Notice of Allowance is also respectfully requested for the withdrawn claims. Should any questions or issues arise concerning the application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

With a request for a one month extension of time and payment of the corresponding fee, this response is due on or before May 16, 2008. The Commissioner is hereby authorized to charge payment of any additional fees that may be required, or credit any overpayment of same, to Deposit Account No. 08-1935, Reference No. 2488.031.

Respectfully submitted,

Dated: May 15, 2008

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